Remarks

I. Status and Nature of the Amendments

Applicants have requested the re-entry of claims 2-4, and their subsequent withdrawal, in order to clarify that these claims have been withdrawn rather than cancelled. Accordingly, as indicated in the Official action, claims 1-31 are presently pending in this application, and claims 32-62 have been cancelled. Due to Applicants' election of the species "cytokine," claims 2-4, 10-15 and 18-25 have been temporarily withdrawn from consideration. Thus, only claims 1, 5-9, 16, 17, and 26-31 have been examined.

Applicants have amended the specification in order to recite the art-recognized definitions for the acronyms presented in claim 17. No new matter has been added by this amendment.

Applicants have also amended claim 1 to more clearly recite that the computer system acts to independently cause the computer system to compare generated data from the assays of the target analytes to data corresponding to the light signal generated by a known concentration of a target analyte and to determine whether the detected signal is within the known dynamic range of the detector's ability to assay that target analyte. The claims further recite that such a goal is accomplished by causing the computer system to vary the detection time duration relative to an initial detection time duration until the detected signal for such analyte is within the known dynamic range of said detector's assay for that target analyte, so as to ensure that the light signal detected by said CCD camera that is used to determine said reported presence, absence, activity or concentration of each target analyte is within said known dynamic range of said assay for that target analyte.

Support for these recitations can be found, *inter alia*, at page 5, line 22 – page 6, line 6, page 31, lines 11–15, page 14, lines 22-24, and in Figures 1–3. No new matter has been added by this amendment.

II. The Rejection of Claim 17 Under 25 U.S.C. § 112, Second Paragraph

Claim 17 has been rejected under 25 U.S.C. § 112, second paragraph in light of its use of acronyms. Specifically, the Examiner has advised that although the claim terms (such as IL, Ron, VEGF, CMCSF, etc. possess art-recognized meanings, it is unclear whether applicant intends to claim the prior art definitions. The Examiner has advised that the terms should be defined in their first instance.

Applicants have indeed intended that the recited terms should possess their art-recognized definitions, and have responded to the Examiner's concerns by amending the specification to recite such art-recognized definitions of the cited terms. Applicants respectfully submit that such amendment fully responds to the Examiner's concerns, and that the rejection may be properly withdrawn.

III. The Rejection of Claims 1, 5-9, 29 and 31 under 25 U.S.C. § 102(e) in Light of Herron *et al.* (U.S. 6,287,871)

Claims 1, 5-9, 29 and 31 have been rejected under 25 U.S.C. § 102(e) in light of Herron *et al.* (U.S. Patent No. 6,287,871). Applicants respectfully traverse and request reconsideration in light of the amended claims.

Applicants respectfully submit that a recited aspect of the present invention relates to the capacity of the invention to determine the presence, absence, activity or concentration of each of multiple target analytes present in a sample. As claimed, the invention accomplishes this feat by independently detecting a signal generated by each analyte and then varying the duration of signal detection until the detected signal is within the dynamic range of the detector's assay for that analyte.

Thus, the claims recite that in the present invention, the presence, absence, activity or concentration of two or more target analytes is independently assayed by causing the "computer system to compare said generated data-to data corresponding to the light signal generated by a known concentration of said target analyte *and to determine whether said*

detected signal is within the known dynamic range of said detector's ability to assay that target analyte." Where the detected signal is outside the known dynamic range of the detector's assay for a target analyte, the claimed method causes the computer system "*to vary the detection time duration relative to an initial detection time duration until the detected signal for an analyte is within the known dynamic range of said detector's assay for that target analyte*" so that, "*for each target analyte being assayed the presence, absence, activity or concentration of such target analyte is determined using data corresponding to a light signal that is within the dynamic range of the detector's assay for that target analyte.*"

Applicants respectfully submit that the presently claimed invention thus differs in at least two salient respects from the method disclosed by Herron *et al.*:

1. Herron *et al.* do not teach that the reported presence, absence, activity or concentration of each target analyte is to be determined using the emissions or quenchings of light signals falling ***within the known dynamic range of the detector's assay for that target analyte***; and

2. Herron *et al.* teach only the passive use of a CCD detection means, and do not teach using a computer system **to ensure** that the concentration of an analyte is calculated with reference signals generated from within the dynamic range of the detector's assay for a target analyte;

Before discussing the basis for each of these differences, Applicants respectfully submit that a description of the method and devices taught by Herron *et al.* would be desirable, and respectfully draw the Examiner's attention to Figure 3 of Herron *et al.* This figure describes a multi-well chamber, in which each chamber contains a blank well, one or more sample wells, and one or more reference wells. The blank well ("well B") lacks the analytes to be assayed. Each reference well ("well R") contains a known concentration of one or more of the analytes to be assayed. Each sample well ("well S") contains an unknown concentration of the one or more analytes being assayed. Additionally, each well is divided

into "patches." Each patch is coated with a binding molecule specific for one of the analytes being assayed.

The method of Herron *et al.* thus operates by using a CCD camera to receive the signal emitted at patch 1 (assaying a first analyte) of well S, so that such signal can be compared with the signals generated at patch 1 of wells R and B (see, for example, column 4, lines 27-31 of Herron *et al.*). The effectiveness of this approach is dependent upon the requirement that each analyte being assayed be present in the sample at a concentration that would lie within the dynamic range of the assay being used for that analyte.

With respect to the above-stated first salient difference between the method of Herron *et al.*, and the present invention, Applicants respectfully submit that the method of Herron *et al.* does not address how the requirement that each analyte being assayed be present in the sample at a concentration that would lie within the dynamic range of the detector being used to assay that analyte may be satisfied. In this regard, the Examiner's attention is directed to the data presented in Figures 13 or 14. Comparing, for example, Figures 13A, 13D, 13G, and 13J, it is apparent that the dynamic range of the assay for ovalbumin reports a signal of 6,000 – 9,000 fluorescence units over a concentration range of 20 – 100 ng in 5 minutes, a value ***wildly*** inconsistent with the fluorescence that should be observed for samples of 0, 20, and 100 ng/ml ovalbumin presented in Figures 13G, 13A, and 13D, respectively. Indeed, had Herron *et al.* not expressly reported the concentrations of ovalbumin in the samples as being 0, 20, and 100 ng/ml ovalbumin, respectively, these concentrations could **not** be determined by those of ordinary skill using the detector data and standard curve provided by Herron *et al.* A similar inability exists as to all data presented in Figures 13 and 14 of Herron *et al.*

Thus, as indicated in Applicants' response to the prior Official Action, in the approach taken by Herron *et al.*, the CCD camera merely reports the signal elicited by the analytes being assayed. If the concentration of an analyte is below (or above) the dynamic range of the detector, the CCD data will provide an inaccurate report of the true concentration of the analyte (as is the case in Figures 13 and 14). The experimentalist would need to repeat the

assay (or equivalently, conduct multiple assays in parallel) in which the assay time was increased, or the analyte diluted. It is thus apparent that the method of Herron *et al.* does not teach determining the concentration of each target analyte using the emissions or quenchings of light signals falling *within the known dynamic range of the detector's assay for that target analyte.*

With respect to the above-stated second salient difference between the method of Herron *et al.*, and the present invention, Applicants respectfully submit that Herron *et al.* fails to disclose or suggest that the dynamic range of an assay can be enhanced through the use of a computer system that has the ability to vary the duration of signal detection independently for each analyte being detected. In this regard, Herron *et al.* teach only that the disclosed assays are to be performed for a particular singular time interval (e.g., 5 minutes; Figures 13 and 14, column 18, lines 10-17), and in the presence of a reference well whose analyte concentration exceeds the concentration of analyte in the sample well (see column 16, lines 14-24).

Applicants thus submit that Herron *et al.* do not address the possibility that different analytes might be present in the sample at concentrations that would fail to fall within a dynamic assay range in the time interval of the assay. At most, Herron *et al.* merely provide that additional zones may be used to test for the concentration of the same analyte (See, column 11, lines 1-2). Herron *et al.* do not, however, disclose or suggest using the signal obtained by the CCD detector to independently vary the detection time for each analyte in order to cause the generated signal for each analyte to fall within the dynamic range of the detector's assay being used to measure that analyte. It is therefore respectfully submitted that the present claims are not anticipated by the Herron *et al.* patent. Applicants therefore respectfully submit that the rejection of claims 1, 5-9, 29 and 31 as anticipated by Herron *et al.* may be properly withdrawn.

IV. The Rejection of Claims 16, 17, 27, 28 and 30 Under 25 U.S.C. § 103(a)

A. The Rejection of Claims 16 and 17 In Light of Herron *et al.* (U.S. 6,287,871) In View of Lehman *et al.* (U.S. 5,939,281)

The teachings of the Herron *et al.* Patent (U.S. 6,287,871) have been discussed above. The Lehman *et al.* Patent (U.S. 5,939,281) is stated to disclose the use of specific binding reagents, such as antibodies, for detecting the concentration of a cytokine. Applicants submit that the combined teachings of the cited references fail to render obvious the present invention since they do not disclose or suggest the claimed use of a computer system to compare the signal elicited by an analyte of unknown concentration with the signal that would be elicited by that analyte within the dynamic range of the assay being used, and to independently alter the duration of signal detection for each assay to ensure that the detected signal falls within the dynamic range of that assay.

Accordingly Applicants respectfully submit that the cited Lehman *et al.* Patent fails to remedy the deficiency of the primary reference, and that the combined references thus fail to render Claims 16 and 17 obvious. Applicants therefore submit that the rejection of Claims 16 and 17 under 35 U.S.C. § 103(a) in light of Herron *et al.* (U.S. 6,287,871) and Lehman *et al.* (U.S. 5,939,281) may be properly withdrawn.

B. The Rejection of Claims 27 and 28 In Light of Herron *et al.* (U.S. 6,287,871) In View of Campbell *et al.* (U.S. 4,946,958)

The teachings of the Herron *et al.* Patent (U.S. 6,287,871) have been discussed above. The Campbell *et al.* Patent (U.S. 4,946,958) is stated to disclose the use of a chemiluminescent label in the analysis, assay or location of proteins. As in the case of the Lehman *et al.* Patent, Applicants submit that the combined teachings of the Herron *et al.* Patent and the Campbell *et al.* Patent fail to render obvious the present invention since they do not disclose or suggest the claimed use of a computer system to compare the signal elicited by an analyte of unknown concentration with the signal that would be elicited by that analyte within the dynamic range of the assay being used, and to independently alter the duration of

signal detection for each assay to ensure that the detected signal falls within the dynamic range of that assay.

Applicants therefore submit that the rejection of Claims 27 and 28 under 35 U.S.C. § 103(a) in light of Herron *et al.* (U.S. 6,287,871) and Campbell *et al.* Patent (U.S. 4,946,958) may be properly withdrawn.

C. The Rejection of Claim 30 In Light of Herron *et al.* (U.S. 6,287,871) In View of McMillan *et al.* (U.S. 6,057,163)

The teachings of the Herron *et al.* Patent (U.S. 6,287,871) have been discussed above. The McMillan *et al.* Patent (U.S. 6,057,163) is stated to disclose the use of a microwell plate for detecting the amount of light emitted by a plurality of samples. As in the case of the Lehman *et al.* and Campbell *et al.* Patents, Applicants submit that the combined teachings of the Herron *et al.* Patent and the McMillan *et al.* Patent fail to render obvious the present invention since they do not disclose or suggest the claimed use of a computer system to compare the signal elicited by an analyte of unknown concentration with the signal that would be elicited by that analyte within the dynamic range of the assay being used, and to independently alter the duration of signal detection for each assay to ensure that the detected signal falls within the dynamic range of that assay.

Applicants therefore submit that the rejection of Claim 30 under 35 U.S.C. § 103(a) in light of Herron *et al.* (U.S. 6,287,871) and McMillan *et al.* (U.S. 6,057,163) may be properly withdrawn.

V. Concluding Remarks

Having now responded to all of the Examiner's rejections, Applicants respectfully submit that the present application is in condition for Allowance, and earnestly solicit early notice of such favorable action. The Examiner is respectfully invited to contact the undersigned with respect to any issues regarding this application.

Respectfully Submitted,

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